UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/535,442	05/19/2005	Stina Roth	014975-119	8832

21839 7590 07/21/2008

BUCHANAN, INGERSOLL & ROONEY PC
POST OFFICE BOX 1404
ALEXANDRIA, VA 22313-1404

EXAMINER	
POHNERT, STEVEN C	

ART UNIT	PAPER NUMBER
1634	

NOTIFICATION DATE	DELIVERY MODE
07/21/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ADIPFDD@bipc.com

Office Action Summary	Application No.	Applicant(s)	
	10/535,442	ROTH ET AL.	
	Examiner	Art Unit	
	Steven C. Pohnert	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 19-24* is/are pending in the application.

4a) Of the above claim(s) *6,11,12,15 and 19-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-10,13,14,23 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 May 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/2/2008 has been entered.

Claim status

Claims 1-15, 19-24 are pending.

Claims 6, 11-12, 15, 19-22 are withdrawn.

Claims 1-5, 7-10, 13-14, 23-24 are being examined.

It is noted that claim 14 has improperly been identified as previously presented, however as noted in the Notice of non-compliant amendment mailed 4/18/2008, claim 14 has been withdrawn from consideration as a non-elected invention. However, in interest of customer service and compact prosecution the application is being examined. However, failure to provide correct claim identifiers in future actions will result in a Non-compliant amendment.

Claim Objections

This objection has been maintained.

Claim 5 is objected to because they specifically recite nonelected subject matter. The claims require “a combination of oligonucleotide probes comprises all or a portion

of the sequences identified with SEQ ID No 1 to 69". As stated in the response to the restriction filed 11/17/2006, applicant has elected a specific combination of SEQ ID NO 24. Applicant should amend the claims so that the claims are directed to the elected invention of the specific combination of genes.

Prior to allowance of these claims, the non-elected subject matter will be required to be deleted from the claims.

Response to Arguments

The response has requested the objection to claim 5 be held in abeyance until allowable matter be determined. Thus as no arguments have been presented this objection is maintained.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-5, 7-10, 13-14, 23-24 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This is a new grounds of rejection presented for the first time.

Claim 1 recites the limitation " said detection " in step c. There is insufficient antecedent basis "said detection" for this limitation in the claim. This rejection can easily be overcome by amending the claim to recite, "detection of said hybridization complex."

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-2, and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Haung (US Patent 5,645,994, Issued 1997).

This rejection is maintained but rewritten to clarify the rejection.

Claim 1 recites, “complementary” in reference to SEQ ID NOs 76 and 77. The recitation of complementary is broadly interpreted to require a single nucleotide that is complementary. If applicant intends the claim require a sequence that is complementary to every nucleotide of SEQ ID NO 76 and 77, the claim should be amended to recite, "completely complementary to the sequence." It is noted that applicant should provide support in the specification for language of such an amendment to insure the amendment meets the Written description requirement.

With regards to claim 1, Huang teaches a method of identifying species of bacteria in a sample by amplification with universal primers based on consensus amino acid sequences which flank variable amino acid sequences (see abstract). Haung further teaches a method of designing universal primer that amplify parE and gyrB (see column 6 lines 28-65), these universal primers would identify the sequences that SEQ ID NO 76 and 77 would identify and comprise complements of SEQ ID NO 76 and 77.

Haung further teaches the use of universal primer compositions to amplify gyrB and parE sequences (see column 14, lines 16-19). Haung further teaches the use of nested primers to specifically distinguish between closely related species (see column 15 lines 27-35). The nested probes are thus the equivalents of the probes claimed.

Haung thus teaches a method of amplification and identification of bacterial species by hybridizing of nested primers with amplification products from universal primers. The nested primers of Haung are used to identify specific species of bacteria, and are thus equivalent to the probes of the claim. Haung's method of nested PCR is contacting amplification products with a desired number of oligonucleotide probes, and detection of hybridization complexes would be the presence of extension products.

With regards to claim 2, Haung further teaches the use of universal primer compositions to amplify gyrB and parE sequences due to their sequence similarities (see column 14, lines 16-19). Haung further teaches identification of legionella pneumophila (SEQ ID NO 70), which is a bacteria that infects the respiratory tract.

With regards to claim 4, Haung et al teaches the use of primers of 15 to 36 nucleotides in length (see column 7, lines 22-25).

Response to arguments

The response asserts, "In particular, a person of ordinary skill in the art would readily recognize that a "complementary sequence" is, by definition, a nucleic acid base sequence that can form a double-stranded structure with a first sequence (the sequence to which the "complementary sequence" is the complement) by matching base pairs. Furthermore, each and every nucleotide in a "complementary sequence," unless

otherwise defined, is complementary to the corresponding nucleotide of such first sequence. For example, the complementary sequence to the DNA sequence AGTCATG must be TCAGTAC, and visa versa. In addition, defining the "percent identity" is not relevant in the context of the present claims, because a "complementary sequence" does not necessarily include any sequence identity to the strand to which it is the complement. “

First, MPEP 716.01(c) makes clear that "The arguments of counsel cannot take the place of evidence in the record. In re Schulze , 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long - felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant." Here, the statements regarding the definition of a complementary sequence are not supported by evidence, however the examiner concurs that complementary sequence requires a nucleic acid sequence that will form a double helix. However, there is no art accepted definition that requires every nucleotide to correspond to a complementary sequence, but only a portion to be complementary and form a double helix. The examiner has suggested language that if supported by the specification would limit the claims to sequences that are completely complementary to the claimed SEQ ID NO.

This should not be construed as an invitation for providing evidence. As further stated in the MPEP 716.01 regarding the timely submission of evidence:

A) Timeliness.

Evidence traversing rejections must be timely or seasonably filed to be entered and entitled to consideration. In re Rothermel, 276 F.2d 393, 125 USPQ 328 (CCPA 1960). Affidavits and declarations submitted under 37 CFR 1.132 and other evidence traversing rejections are considered timely if submitted:

(1) prior to a final rejection,

(2) before appeal in an application not having a final rejection, or

(3) after final rejection and submitted

(i) with a first reply after final rejection for the purpose of overcoming a new ground of rejection or requirement made in the final rejection, or

(ii) with a satisfactory showing under 37 CFR 1.116(b) or 37

CFR 1.195, or

(iii) under 37 CFR 1.129(a).

This rejection is maintained.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claim 3, 7, 8, 10, 13, are rejected under 35 U.S.C. 103(a) as being unpatentable over Haung (US Patent 5645994, Issued 1997) in view of Voelker (US patent publication 2004/0048281, filed March 23, 2001).

This rejection is maintained.

Huang teaches a method of identifying species in a sample by amplification with universal primers based on consensus amino acid sequences which flank variable amino acid sequences (see abstract). Haung further teaches a method of designing universal primer (see column 6 lines 28-65); these universal primers are minimally, functional fragments that identify the sequence that SEQ ID NO 76 and 77 detect. Haung further teaches the use of universal primer compositions to amplify gyrB and parE sequences (see column 14, lines 16-19). Haung further teaches the use of nested primers to specifically distinguish between closely related species (see column 15 lines 27-35).

Haung does not teach the amplification of the hypervariable region of gyrB or parE in Staphylococcus aureus. Haung does not teach the use of a solid support.

However, Voelker et al teaches amplification of gram-positive bacteria, Staphylococcus aureus gyrB (see figure 1B, lane 3, and paragraph 0025) and parE (see figure 2B, lane 3, and paragraph 0026). Voelker teaches that most clinical samples are from gram-positive bacteria (see paragraph 0004). Voelker teaches the use of degenerate primers for the identification of quinolone resistance determining regions across phylogenetic ranges of prokaryotes (see paragraph 0001, last sentence) for diagnosis, prognosis, therapy and drug discovery (see paragraph 0024).

Further, Voelker et al teaches, "a solid surface on which is immobilized at pre-defined regions thereon a plurality of defined oligonucleotide/polynucleotide sequences for hybridization and identification." The solid surface with immobilized probes is a microarray (see paragraph 0024).

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the Haung method of detecting bacterial species to amplify gyrB and parE to identify Staphylococcus aureus and use a solid support as taught by Voelker. The ordinary artisan would be motivated improve Haung's method of bacterial detection to identify Staphylococcus aureus and use solid supports as taught Voelker because Voelker teaches gram positive bacteria are the most clinically relevant. This would allow proper diagnosis and treatment of these gram-positive bacteria. Further the use of the probes on solid supports as Voelker teaches would decrease the use of reagents and increase the speed of detection.

Response to arguments

The response has presented no arguments to the instant 103. The arguments to the 102 based on Haung have been addressed above. The rejection is thus maintained.

8. Claims 4, 5 and 23 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haung (US Patent 5645994, Issued 1997) in view of Hogan et al (US Patent 5541308) and Hopewell et al (Journal of Bacteriology (1990), volume 172, pages 3481-3484).

This rejection has been maintained.

Huang teaches a method of identifying species in a sample by amplification with universal primers based on consensus amino acid sequences, which flank variable amino acid sequences (see abstract). Haung further teaches a method of designing universal primer (see column 6 lines 28-65), these universal primers are minimally, functional fragments of SEQ ID NO 76 and 77. Haung further teaches the use of universal primer compositions to amplify gyrB and parE sequences (see column 14, lines 16-19

Haung does not teach the probe of the comprising all or a portion of SEQ ID NO 24.

However, Hogan et al teaches probe design for detection of specific sequences (see abstract). Hogan teaches identification of variable regions (see column 6, lines 3-55). Hogan teaches alignment of these variable regions (see column 6 line 67—column 7, line 8). Hogan further teaches probes should be positioned to minimize stability of probe:nontarget hybrids, by avoiding GC rich regions and areas of frequent mutation (see column 7 lines 10-15). Hogan teaches the use of synthetic oligonucleotide probes of 15-50 base pairs (see column 10, lines 40-45). Hogan further teaches maximizing stability of probe target hybrid, by avoiding long AT sequences and terminating hybrids with G:C base pairing and the appropriate T_m(see column 7 lines 16-19). Hogan further teaches targeting sequences known to have secondary structure issues and probes that are self-complementary should be avoided (see column 7, lines 20-29).

Hopewell teaches sequence of Staphylococcus aureus gyrB, which comprises SEQ ID NO 24, (see figure 3B). Hopewell teaches that quinolone resistant

Staphylococcus aureus are a major medical problem and this resistance is due to mutations in the DNA gyrase enzyme (see page 3481, 1st column, 1st paragraph).

Designing probes, which are equivalents to those taught in the art is routine experimentation. The prior art teaches the parameters and objectives involved in the selection of oligonucleotides that function as probes, see Hogan. Moreover there are many internet web sites that provide free downloadable software to aid in the selection of probes drawn from genetic data recorded in a spreadsheet. The prior art is replete with guidance and information necessary to permit the ordinary artisan in the field of nucleic acid detection to design probes As discussed above, the ordinary artisan would be motivated to have designed and tested new probes to obtain additional oligonucleotides that function to detect specific hypervariable regions of bacteria and identify oligonucleotides with improved properties. The ordinary artisan would have a reasonable expectation of success of obtaining additional probes from within the sequences provided by Haung. Thus, for the reasons provided above, the ordinary artisan would have designed additional probes using the teachings in the art at the time the invention was made. The claimed SEQ ID NOs are obvious over the cited prior art, absent secondary considerations.

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the sequences taught by Hopewell and the probe design method of Hogan to make probes to detect bacterial species based on the gyrB. The ordinary artisan would thus design a probe comprising SEQ ID NO 24 or a functional fragment of SEQ ID NO 24. The ordinary artisan would be motivated to use

the sequence taught by Hopewell to design probes by Hogan's method of probe design to identify mutations that result in quinolone resistance because Hopewell teaches this is a serious medical problem and proper identification would allow efficient treatment.

Response to arguments

The response has presented no arguments to the instant 103. The arguments to the 102 based on Haung have been addressed above. The rejection is thus maintained.

9. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Haung (US Patent 5645994, Issued 1997) and Voelker (US patent publication 2004/0048281, filed March 23, 2001) as applied to claim 7 above, and further in view of Southern et al (Nature Genetics supplement (1999), volume 21 pages 5-9).

This rejection has been maintained.

The teachings of Haung in view of Voelker are set forth above.

Haung and Voelker teach the use of a solid support, however they do not teach the use of treated glass as a solid substrate.

Southern et al teach that treated glass is a preferred solid support as it allows the synthesis of oligonucleotides (see page 7, 1st column line 30-36). Southern teaches that the use of glass has the advantages that liquid cannot penetrate glass, it enhances the rate of hybridization, improves washing by improving diffusion.

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the treated glass support taught by Southern as the solid support of Haung in view of Voelker. The ordinary artisan would

be motivated to use the treated glass support of Southern because Southern teaches glass improves washing; rate of hybridization and liquid cannot penetrate it. The use of the treated glass taught by Southern would thus allow more efficient assays.

Response to arguments

The response has presented no arguments to the instant 103. The arguments to the 102 based on Haung have been addressed above. The rejection is thus maintained.

10. Claims 1-4, 7-10, 13, 23-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haung (US Patent 5,645,994, Issued 1997) in view of Haselbeck et al (WO01/70955, published September 27, 2001).

This is a New Grounds of rejection drawn to the interpretation that the claims require primers comprising SEQ ID NO 76 and 77 or sequences that are completely complementary to SEQ ID NO 76 and 77.

It is noted that claim 5 recites, "oligonucleotide probes comprise all or a portion of sequences identified with SEQ ID NO 1 to 69." This recitation is being given the broadest reasonable interpretation that the claim requires a portion of the elected SEQ ID NO 24, which includes a single nucleic acid.

With regards to claim 1, Huang teaches a method of identifying species of bacteria in a sample by amplification with universal primers based on consensus amino acid sequences which flank variable amino acid sequences (see abstract). Haung further teaches a method of designing universal primer that amplify parE and gyrB (see column 6 lines 28-65), these universal primers would identify the sequences that SEQ

ID NO 76 and 77 would identify and comprise complements of SEQ ID NO 76 and 77. Haung further teaches the use of universal primer compositions to amplify gyrB and parE sequences (see column 14, lines 16-19). Haung further teaches the use of nested primers to specifically distinguish between closely related species (see column 15 lines 27-35). The nested probes are thus the equivalents of the probes claimed. Haung further teaches, "In theory, a single pair of primers, one from each flanking consensus sequence, can be used to amplify the signature sequence. However, a highly preferred embodiment includes a multiplicity of primers having sequences corresponding to potential alternate DNA sequences. As is well-known, the genetic code is degenerate, meaning that an individual amino acid may be coded for by as many as 6 different DNA codons (each codon consisting of three adjacent nucleotides). Thus, even though the amino acid sequence of a region of type II topoisomerase from different organisms may be identical, the DNA in those organisms which codes for the region may differ. The PCR technique requires a good match between the DNA primer sequences especially at the 3' end and the DNA to which it binds (Saiki et al.). Thus, to avoid failing to amplify species having such alternate DNA sequences, the set of primers should include variant primers having at least some of the alternate sequences. Moreover, it is desirable that the amino acids in the consensus sequence be coded for by 3 or fewer different codons, especially in the portion immediately adjacent to the signature segment. Obviously, the presence of one or more amino acids having six possible codons drastically increases the number of possible DNA sequences. By choosing the consensus sequences to have amino acids with at most three possible codons (or in an even more preferred

embodiment, two possible codons), the number of different oligonucleotide sequences required in the universal primers is kept manageable" (see column 7, line 60 to column 8, line 9). Huang teaches, "t will be recognized that universal primers such as the compositions described herein can be constructed for any ubiquitous protein having substantially conserved segments adjacent to variable segments. Depending upon the desired application, gene products other than type II topoisomerase might be preferable. Examples of proteins of potential use according to this invention include RNA polymerase and other DNA binding proteins. Where it is desired only to distinguish among very closely related species, a protein common only to such species may be used" (see column 14, lines 46-50). Huang concludes, "it will be apparent how a specific primer pair for any species can be designed by the methods disclosed herein and using a database" (see column 16, lines 50-55).

With regards to claim 2, Haung further teaches the use of universal primer compositions to amplify gyrB and parE sequences due to their sequence similarities (see column 14, lines 16-19). Haung further teaches identification of legionella pneumophila (SEQ ID NO 70), which is a bacteria that infects the respiratory tract.

With regards to claim 3, Huang teaches detection of pseudomonase aeruginosa (see figure 9 a).

With regards to claim 4, Haung et al teaches the use of primers of 15 to 36 nucleotides in length (see column 7, lines 22-25).

With regards to claims 23 and 24 Huang et al teaches primers of 24 bases (see SEQ ID NO 206 and SEQ ID NO 207).

Huang does not teach primers comprising SEQ ID NO 76 and 77 or primers comprising the full complement of SEQ ID NO 76 and SEQ ID NO 77.

However, Haselbeck et al teaches SEQ ID NO 9244, which contains nucleotides 82 to 101 that comprise SEQ ID NO 76 of instant claims. Haselbeck further teaches SEQ ID NO 1844, which contains nucleotides 14 to 33 which comprise SEQ ID NO 77. Haselbeck teaches, "The identified or isolated nucleic acids obtained using the PCR primers may contain part or all of the homologous nucleic acids. Because homologous nucleic acids are related but not identical in 25 sequence, those skilled in the art will often employ degenerate sequence PCR primers. Such degenerate sequence primers are designed based on sequence regions that are either known to be conserved or suspected to be conserved such as conserved coding regions. The successful production of a PCR product using degenerate probes generated from the sequences identified herein would indicate the presence of a homologous gene sequence in the species being screened. The PCR primers 30 are at least 10 nucleotides, and preferably at least 20 nucleotides in length. More preferably, the PCR primers are at least 20-30 nucleotides in length. In some embodiments, the PCR primers can be more than 30 nucleotides in length. It is preferred that the primer pairs have approximately the same G/C ratio, so that melting temperatures are approximately the same." (see page 232, lines 23-33). Haselbeck teaches multiple nucleic acid sequences that comprise a multiple nucleotides that are broadly interpreted as a portion of SEQ ID No 24.

With regards to claims 7-9, Haselbeck teaches, "In another embodiment, gene expression arrays and microarrays can be employed. Gene expression arrays are high

density arrays of DNA samples deposited at specific locations on a glass chip, nylon membrane, or the like. Such arrays can be used by researchers to quantify relative gene expression under different conditions. Gene expression arrays are used by researchers to help identify optimal drug targets, profile new compounds, and determine disease pathway" (see page 78, lines 1-5).

With regards to claim 10, Haselbeck teaches use of a single stranded labeled probe (see page 231, lines 5-20).

With regards to claim 10, Haselbeck teaches the use of nucleic acid probes to identify microorganism species from clinical specimens (see page 195, line 20). Haselbeck further teaches, "Single stranded labeled cDNAs are prepared for hybridization to the array" (see page 149, line 17)

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the method of Huang with the nucleic acids taught by Haselbeck which comprise SEQ ID NO 76 and 77. The skilled artisan would be motivated to combine the teachings of Huang and Haselbeck because Huang suggests the use of his method with any protein and any sequence in a database for identification of bacteria. The skilled artisan would also be motivated to combine the teachings of Huang and Haselbeck because Haselbeck suggests the use of his method to identify microorganism species.

It would further have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use arrays or microarrays in the combined method

of Huang and Haselbeck because Haselbeck teaches it allows the detection of multiple gene expression products and thus markers.

The artisan would have a reasonable expectation of success in combining the teachings of Huang and Haselbeck as both teach methods of identifying microorganism by hybridization using methods and techniques known in the art.

11. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Haung (US Patent 5,645,994, Issued 1997) in view of Haselbeck et al (WO01/70955, published September 27, 2001) as applied to claims 1-5, 7-10, 13, 23-24 above, and further in view of Hogan et al (US Patent 5541308) and Hopewell et al (Journal of Bacteriology (1990), volume 172, pages 3481-3484).

This rejection is drawn to the interpretation claim 5 requires a probe comprising the entire elected sequence of SEQ ID NO 24 or a sequence that is fully complementary to SEQ ID NO 24.

The teachings of Huang and Haselbeck are set forth in paragraph 10 above.

Haung and Haselbeck do not teach the probe of the comprising all or a portion of SEQ ID NO 24.

However, Hogan et al teaches probe design for detection of specific sequences (see abstract). Hogan teaches identification of variable regions (see column 6, lines 3-55). Hogan teaches alignment of these variable regions (see column 6 line 67—column 7, line 8). Hogan further teaches probes should be positioned to minimize stability of probe:nontarget hybrids, by avoiding GC rich regions and areas of frequent mutation (see column 7 lines 10-15). Hogan teaches the use of synthetic oligonucleotide probes

of 15-50 base pairs (see column 10, lines 40-45). Hogan further teaches maximizing stability of probe target hybrid, by avoiding long AT sequences and terminating hybrids with G:C base pairing and the appropriate T_m(see column 7 lines 16-19). Hogan further teaches targeting sequences known to have secondary structure issues and probes that are self-complementary should be avoided (see column 7, lines 20-29).

Hopewell teaches sequence of Staphylococcus aureus gyrB, which comprises SEQ ID NO 24, (see figure 3B). Hopewell teaches that quinolone resistant Staphylococcus aureus are a major medical problem and this resistance is due to mutations in the DNA gyrase enzyme (see page 3481, 1st column, 1st paragraph).

Designing probes, which are equivalents to those taught in the art is routine experimentation. The prior art teaches the parameters and objectives involved in the selection of oligonucleotides that function as probes, see Hogan. Moreover there are many internet web sites that provide free downloadable software to aid in the selection of probes drawn from genetic data recorded in a spreadsheet. The prior art is replete with guidance and information necessary to permit the ordinary artisan in the field of nucleic acid detection to design probes As discussed above, the ordinary artisan would be motivated to have designed and tested new probes to obtain additional oligonucleotides that function to detect specific hypervariable regions of bacteria and identify oligonucleotides with improved properties. The ordinary artisan would have a reasonable expectation of success of obtaining additional probes from within the sequences provided by Haselbeck using the method described by Hogan and Huang. Thus, for the reasons provided above, the ordinary artisan would have designed

additional probes using the teachings in the art at the time the invention was made. The claimed SEQ ID NOs are obvious over the cited prior art, absent secondary considerations.

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the sequence taught by Hopewell and the probe design method of Hogan to make probes to detect bacterial species based on the gyrB. The ordinary artisan would thus design a probe comprising SEQ ID NO 24 or complementary to SEQ ID NO 24. The ordinary artisan would be motivated to use the sequence taught by Hopewell to design probes by Hogan's method of probe design to identify mutations that result in quinolone resistance because Hopewell teaches this is a serious medical problem and proper identification would allow efficient treatment. The artisan would have a reasonable expectation of success as the methods are drawn to well known methods of making and analyzing nucleic acids known in the art.

Summary

No claims are allowed over prior art cited.

Conclusions

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven C. Pohnert whose telephone number is 571-272-3803. The examiner can normally be reached on Monday-Friday 6:30-4:00, every second Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Steven Pohnert

/Sarae Bausch/
Primary Examiner, Art Unit 1634